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II. REMARKS

Before the amendments made herein, claims 1, 5-13, and 16-36 were pending. Claim 37 has been added herewith. Accordingly, after entry of the amendments made herein, claims 1, 5-13, and 16-37 will be pending.

A. Regarding the amendments

Claim 1 has been amended to more clearly indicate that, while the recited agent includes an oligosaccharide of up to about 10 saccharide units, with these units the oligosaccharide comprises the recited disaccharide. The amendment is supported in the specification, for example, at page 9, lines 19-20.

Claim 37 has been added and requires that the recited oligosaccharide have a molecular weight of no more than about 300 daltons. The new claim is supported in the specification, for example, at page 20, line 3.

Because the amendments made herein are fully supported by the specification, no issue of new matter arises.

B. Regarding the indefiniteness rejection

The claims are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. More specifically, the Action points out that claim 1 recites that the claimed agent "consists of" an oligosaccharide of up to about 10 saccharide units, and that the oligosaccharide also "comprises" the claimed disaccharide of formula (I). The Action alleges that the metes and bounds of the claim cannot be ascertained by the skilled artisan because both closed-ended and open-ended terminology is being used. Applicants respectfully traverse the rejection.

To more clearly indicate the claimed subject matter, claim 1 has been amended herein to recite that, while the claimed agent consists of an oligosaccharide of up to about 10 saccharide units, within said units comprises (i.e., includes) a disaccharide of formula (I). In view of the clarifying amendment made herein, Applicants submit that the skilled artisan would be able to understand the metes and bounds of the claims. Accordingly, Applicants respectfully request that this rejection be withdrawn.

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C. Regarding the obviousness rejection

Claims 1, 7, 8, 10-12, 16-21, 24, 25, 27, 28, and 30-36 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over U.S. Pat. No. 4,882,318 in view of Vlodavsky et al., Adv. Exp. Med. Biol., 13:317-27 (1992). Applicants respectfully traverse the rejection.

In response to the arguments made by Applicants in the previous response, the Action (on page 6) makes two assertions. The first assertion is that "although Vlodavsky teaches [that] inhibition of tumor metastasis would be best achieved by oligosaccharides with 16 or more sugar units, Vlodavsky does not exclude oligosaccharides with less than 8 units [or that such 8 unit oligosaccharides] would be ineffective in treating tumor metastasis."

In response, Applicants respectfully submit that Vlodavsky teaches absolutely nothing that would motivate the skilled artisan to use oligosaccharides of 10 units or less to treat a malignancy, as required by the subject claims. Indeed, what Vlodavsky teaches about oligosaccharides that are within the scope of the claims would, if anything, motivate the skilled artisan not to employ such sugars to treat a malignancy.

Here is what Vlodavsky teaches about such sugars for treating malignancy: First, Vlodavsky teaches on page 319 that to retain high inhibitory activity against metastasis, the N-substituted oligosaccharides require a molecular size of about 4000 daltons or more. As shown by the attached reference (Venkataraman et al., Science, 286:537-42 (1999), such a molecular size excludes the oligosaccharides of the subject claims (where an 8 unit sugar on page 538 of Venkataraman, for example, has a molecular weight of 2230.2 daltons). Thus, Vlodavsky is teaching that the oligosaccharides within the scope of the subject claims do not retain high inhibitory activity against cancer metastasis.

Moreover, Vlodavsky teaches on page 319 that a pentasaccharide was devoid of inhibitory activity. Thus, given these teachings of Vlodavsky, the skilled artisan would have absolutely no motivation to make the oligosaccharides of the subject invention.

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As an aside, Applicants further note that the Action's assertion that Vlodavsky "does not exclude" the idea that such compounds may be effective in treating tumor metastasis (even if true, which it is not, as discussed above) does not establish a *prima facie* case of obviousness. And the Action has surely not made a *prima facie* case of obviousness against each and every claim under examination, for example, claims 34 and 35, which require a maximum of about 2000 and 1100 daltons, respectively, or claim 36, which does not recite lung cancer.

Secondly, the Action asserts on page 6 that, based on Figure 1 of Vlodavsky, the skilled artisan would have been motivated to "optimize" the length of the sugar units in order to maximize the tumor metastasis effect while minimizing the release of bFGF. Applicants respectfully disagree with this assertion.

On page 321, Vlodavsky teaches that maximal release of bFGF was accomplished with an eight unit oligosaccharide. Moreover, Vlodavsky teaches that, on a weight basis, the higher (e.g., 16) unit oligosaccharides showed similar results as the eight unit oligosaccharide. In view of these teachings, the skilled artisan would not have been motivated to "optimize" the length of the sugar (say to be in the eight-unit range) in order to maximize the tumor metastasis effect while minimizing the release of bFGF. For a sugar in the eight-unit range would have a very high bFGF effect (as discussed above).

Moreover, Vlodavsky makes no teaching whatsoever that such an eight unit sugar would have a high inhibitory effect against metastasis. Indeed, as discussed above, because such an eight unit sugar has a molecular weight of less than 4000 daltons, if anything, Vlodavsky teaches that such a sugar would not have a high inhibitory effect against tumor metastasis.

Furthermore, reading Vlodavsky, the skilled artisan would not have been motivated to use a much shorter sugar to treat a malignancy. While Figure 1 of Vlodavsky shows that such sugars release less bFGF, as discussed above, Vlodavsky also teaches that a sugar with five units had no inhibitory effect whatsoever against tumor metastasis.

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In summary, Vlodavsky provides no motivation whatsoever to use the oligosaccharides as claimed herein to treat a malignancy. To the contrary – Vlodavsky leads the skilled artisan to use sugars of 16 units or longer to treat metastasis, and has only bad things to say about the metastatic inhibitory effect of sugars within the scope of the claimed invention (i.e., sugars with 10 units or less). In addition, because sugars in the eight-unit range showed very high activity in releasing bFGF, the skilled artisan would not have been motivated by Vlodavsky to make sugars in this size range to treat cancer. Finally, the skilled artisan would have had even less motivation to make sugars with less units in view of the fact that Vlodavsky teaches that a five unit sugar was completely devoid of activity against tumor metastasis. For all of these reasons, Applicants respectfully request that this rejection be withdrawn.

III. CONCLUSION

All of the issues raised in the Office Action have been addressed and are believed to have been overcome. Accordingly, it is respectfully submitted that all the claims under examination in the subject application are allowable. Therefore Applicants respectfully request a Notice of Allowance to this effect.

Respectfully submitted,



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Date: January 19, 2006

Encl.

1. Reference (Venkataraman et al., Science, 286:537-42 (1999))
2. Additional Claim Fee